The human gut microbiota is a metabolic organ that is determined by a dynamic process of selection and competition. Age, dietary habits and geographical origin of people have an important impact on the intestinal microbiota. The role of the microbiota is still largely unknown, but the bacteria of the gut flora do contribute enzymes that are absent in humans and play an essential role in the catabolism of dietary fibers. Germ-free mice provide a complementary approach for characterizing the properties of the human gut microbiota. Recently, microbial changes in the human gut were proposed to be one of the possible causes of obesity. This review summarizes the latest research on the association between microbial ecology and host weight.
Review
Phage cocktails and the future of phage therapy

Benjamin K Chan1, Stephen T Abedon2 & Catherine Loc-Carrillo3,4

1Department of Internal Medicine, University of Utah, Salt Lake City, UT, USA
2Department of Microbiology, Ohio State University, Mansfield, OH, USA
3Department of Orthopedics, University of Utah, Salt Lake City, UT, USA
4Department of Veterans Affairs, Health Care System, Salt Lake City, UT, USA

Future Microbiology 8(6), 769–783 (2013).
www.futuremedicine.com/doi/full/10.2217/fmb.11.135

Viruses of bacteria, known as bacteriophages or phages, were discovered nearly 100 years ago. Their potential as antibacterial agents was appreciated almost immediately, with the first ‘phage therapy’ trials predating Fleming’s discovery of penicillin by approximately a decade. In this review, we consider phage therapy that can be used for treating bacterial infections in humans, domestic animals and even biocontrol in foods. Following an overview of the topic, we explore the common practice – both experimental and, in certain regions of the world, clinical – of mixing therapeutic phages into cocktails consisting of multiple virus types. We conclude with a discussion of the commercial and medical context of phage cocktails as therapeutic agents. In comparing off-the-shelf versus custom approaches, we consider the merits of a middle ground, which we deem ‘modifiable’. Finally, we explore a regulatory framework for such an approach based on an influenza vaccine model.

Perspective
Nucleic acids as viability markers for bacteria detection using molecular tools

Claire Cenciariini-Borde1,2, Sophie Courtois1 & Bernard La Scola2

1CIRSEE (Centre International de Recherche Sur l’Eau et l’Environnement) – Suez Environment, 38 Rue Du Président Wilson 78230 Le Pecq, France
2UMR9, CNRS-IRD UMR 6236, Université de la Méditerranée, Faculté de Médecine, 27 Bd Jean Moulin, 13385 Marseille Cedex 05, France

www.futuremedicine.com/doi/full/10.2217/17460913.4.1.45

A large set of nucleic acid detection methods with good sensitivity and specificity are now available for the detection of pathogens in clinical, food and environmental samples. Given increasing demand, many efforts have been made to combine these methods to assess viability. Genomic DNA PCR amplification has been shown to be inappropriate for distinguishing viable from dead bacteria owing to DNA stability. Many authors have tried to bypass this difficulty by switching to RNA amplification methods such as reverse transcription-PCR and nucleic acid sequence-based amplification. More recently, researchers have developed methods combining specific sample pretreatment with nucleic acid detection methods, notably ethidium or propidium monoazide pretreatment coupled with PCR DNA detection or direct viable count methods and subsequent fluorescent in situ hybridization of 16S rRNA. This review evaluates the performance of these different methods for viability assessment.

Review
Insights into antibiotic resistance through metagenomic approaches

Robert Schmieder1 & Robert Edwards1,2

1Computational Science Research Center & Department of Computer Science, San Diego State University, San Diego, CA 92182, USA
2Mathematics and Computer Science Division, Argonne National Laboratory, 9700 South Cass Ave, Argonne, IL 60439, USA

Future Microbiology 7(1), 73–89 (2012).
www.futuremedicine.com/doi/full/10.2217/fmb.11.135

The consequences of bacterial infections have been curtailed by the introduction of a wide range of antibiotics. However, infections continue to be a leading cause of mortality, in part due to the evolution and acquisition of antibiotic-resistance genes. Antibiotic misuse and overprescription have created a driving force influencing the selection of resistance. Despite the problem of antibiotic resistance in infectious bacteria, little is known about the diversity, distribution and origins of resistance genes, especially for the unculturable majority of environmental bacteria. Functional and sequence-based metagenomics have been used for the discovery of novel resistance determinants and the improved understanding of antibiotic-resistance mechanisms in clinical and natural environments. This review discusses recent findings and future challenges in the study of antibiotic resistance through metagenomic approaches.

Review
Tuberculous meningitis in adults: a review of a decade of developments focusing on prognostic factors for outcome

Flavia Brancusi1, Jeremy Farrar2 & Dorothee Heemskerk2

1Princeton University, Princeton, NJ, USA
2Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

Future Microbiology 7(9), 1101–1116 (2012).
www.futuremedicine.com/doi/full/10.2217/17460913.12.86

Tuberculous meningitis (TBM) is the most severe form of TB. Despite treatment, mortality and long-term disability remain unacceptably high. Prevention, early recognition, diagnosis and treatment are fundamental to improving outcomes. However, an effective vaccine remains elusive, initial symptoms are nonspecific, and sensitive diagnostic tests are
not available. There has been progress in our understanding of the immunopathology of TBM, and several factors have been found to be associated with susceptibility to infection, disease progression and clinical outcome. However, these have not yet impacted on treatment. Early treatment initiation and uninterrupted continuation, severity on presentation, seizures, stroke, cranial nerve involvement, cerebrospinal fluid cell count and lactate levels, hyponatraemia and coinfection with HIV are all found to be important prognostic factors for outcome. Pathogen lineage (Beijing genotype) and host genetics (polymorphisms in TLR2, TIRAP and LTA4H genes) can influence susceptibility to TBM. However, these findings have not yet impacted on treatment. Progress in vaccine development, opportunities for better diagnostic tests, novel insights into pathogenesis and an increasing evidence base for improving treatment should impact the current high mortality and morbidity, if translated to global and local guidelines.

Review

Virulence factors involved in the pathogenesis of the infection caused by the swine pathogen and zoonotic agent Streptococcus suis

Nahuel Fittipaldi1, Mariela Segura1, Daniel Grenier2 & Marcelo Gottschalk1

1Groupe de Recherche sur les Maladies Infectieuses du Porc & Centre de Recherche en Infectiologie Porcine, Faculté de médecine vétérinaire, Université de Montréal, 3200 rue Sicotte, C.P. 5000, St-Hyacinthe, Quebec, J2S 7C6, Canada
2Groupe de Recherche en Écologie Buccale, Faculté de Médecine Dentaire, Université Laval, Quebec City, Quebec, Canada

Streptococcus suis is a major swine pathogen responsible for important economic losses to the swine industry worldwide. It is also an emerging zoonotic agent of meningitis and streptococcal toxic shock-like syndrome. Since the recent recognition of the high prevalence of S. suis human disease in southeast and east Asia, the interest of the scientific community in this pathogen has significantly increased. In the last few years, as a direct consequence of these intensified research efforts, large amounts of data on putative virulence factors have appeared in the literature. Although the presence of some proposed virulence factors does not necessarily define a S. suis strain as being virulent, several cell-associated or secreted factors are clearly important for the pathogenesis of the S. suis infection. In order to cause disease, S. suis must colonize the host, breach epithelial barriers, reach and survive in the bloodstream, invade different organs, and cause exaggerated inflammation. In this review, we discuss the potential contribution of different described S. suis virulence factors at each step of the pathogenesis of the infection. Finally, we briefly discuss other described virulence factors, virulence factor candidates and virulence markers for which a precise role at specific steps of the pathogenesis of the S. suis infection has not yet been clearly established.

Review

Postgenomic strategies in antibacterial drug discovery

Heike Brötz-Oesterhelt1 & Peter Sass2

1‘AIC, Wupperland, Germany, Institute for Pharmaceutical Biology, University of Duesseldorf, Universitätsstrasse 1, Building 26.23 U1, Germany
2Institute of Medical Microbiology, Immunology & Parasitology, Pharmaceutical Microbiology Section, University of Bonn, Germany


www.futuremedicine.com/doi/full/10.2217/fmb.10.119

During the last decade the field of antibacterial drug discovery has changed in many aspects including bacterial organisms of primary interest, discovery strategies applied and pharmaceutical companies involved. Target-based high-throughput screening had been disappointingly unsuccessful for antibiotic research. Understanding of this lack of success has increased substantially and the lessons learned refer to characteristics of targets, screening libraries and screening strategies. The ‘genomics’ approach was replaced by a diverse array of discovery strategies, for example, searching for new natural product leads among previously abandoned compounds or new microbial sources, screening for synthetic inhibitors by targeted approaches including structure-based design and analyses of focused libraries and designing resistance-breaking properties into antibiotics of established classes. Furthermore, alternative treatment options are being pursued including anti-virulence strategies and immunotherapeutic approaches. This article summarizes the lessons learned from the genomics era and describes discovery strategies resulting from that knowledge.

Editorial

Ebolavirus: a brief review of novel therapeutic targets

Andrew S Kondratowicz1 & Wendy J Maury1

1Department of Microbiology, Carver College of Medicine, University of Iowa, Iowa City, IA, USA


www.futuremedicine.com/doi/full/10.2217/fmb.11.110

Ebolavirus (EBOV) and Marburgvirus (MARV) are members of the family Filoviridae and contain a single-stranded, negative sense ~19 kb RNA genome. There is a single species of MARV, whereas there are five known species of EBOV: Zaire EBOV, Reston EBOV, Ivory Coast EBOV, Sudan EBOV and Bundibugyo EBOV. While Reston EBOV does not cause disease in humans, the other four species cause Ebola hemorrhagic fever (EHF), with human mortality rates between 40–90% and no vaccines or antivirals are currently available. As disease symptoms are thought to be caused by both replication of the virus and host immune responses, promising future therapies logically would focus on reducing virus load and/or enhancing productive immune responses.
Review
Polio vaccination: past, present and future
Ananda S Bandyopadhyay1, Julie Garon2, Katherine Seib2 & Walter A Orenstein2
1Bill & Melinda Gates Foundation, 1432 Elliott Ave W, Seattle, WA 98119, USA
2Division of Infectious Diseases, Emory University School of Medicine, 1462 Clifton Road, Room 446, Atlanta, GA 30322, USA
www.futuremedicine.com/doi/full/10.2217/fmb.15.19

Live attenuated oral polio vaccine (OPV) and inactivated polio vaccine (IPV) are the tools being used to achieve eradication of wild polio virus. Because OPV can rarely cause paralysis and generate revertant polio strains, IPV will have to replace OPV after eradication of wild polio virus is certified to sustain eradication of all polioviruses. However, uncertainties remain related to IPV’s ability to induce intestinal immunity in populations where fecal–oral transmission is predominant. Although substantial effectiveness and safety data exist on the use and delivery of OPV and IPV, several new research initiatives are currently underway to fill specific knowledge gaps to inform future vaccination policies that would assure polio is eradicated and eradication is maintained.

Editorial
Could fecal microbiota transplantation cure all Clostridium difficile infections?
Thomas J Borody1, Debra Peattie2 & Amit Kapur3
1Centre for Digestive Diseases, Level ½29 Great North Road, Five Dock, New South Wales 2046, Australia
2Pleades Advisors, 13 Oak Meadow Road, Lincoln, MA 01773, USA
3Prince of Wales Hospital, Randwick, New South Wales 2031, Australia
www.futuremedicine.com/doi/full/10.2217/fmb.13.146

In its current form, fecal microbiota transplantation (FMT) is a novel medical therapy. Intriguingly, however, early Chinese writings reveal that it was practiced centuries ago in its crudest form using ingested fecal material to treat gastrointestinal ailments such as food poisoning and severe diarrhea. As we discuss here, this ancient medical practice may now be coming ‘full circle’. In 1958, Eiseman and colleagues documented the first modern report of FMT to treat pseudomembranous colitis due to suspected Clostridium difficile infection (CDI). The authors detailed an “immediate and dramatic response” following FMT and suggested that “this simple yet rational therapy method should be given more extensive clinical evaluation”. Although C. difficile was not described until 1978, the Eiseman et al. report and several others that followed almost certainly described treatments for what we now know to be CDI colitis.